American Journal of Medical Genetics 65:222–225 (1996)

Brief Clinical Report

Possibly New Multiple Congenital Anomaly Syndrome: Cranio-Fronto-Nasal Dysplasia With Poland Anomaly

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We present a possibly new multiple congenital anomaly syndrome of craniosynostosis, Poland anomaly, cranio-fronto-nasal "dysplasia," and genital and breast anomalies. A similar pattern of anomalies was observed in two previous cases from the literature; however, some peculiar findings suggest that these cases might represent a new multiple congenital anomaly syndrome.

KEY WORDS: **frontonasal dysplasia, cranio-fronto-nasal dysplasia, Poland anomaly**

INTRODUCTION

Craniofrontonasal dysplasia (CFND) was first identified by Cohen [1979]. CFND is characterized by frontonasal "dysplasia" (FND (more correctly dysostosis)), coronal craniosynostosis, grooved nails, and variable extracranial anomalies. Most cases are sporadic and female [Morris et al., 1987]. FND, the most important component of the syndrome, is a major midline developmental anomaly, resulting from an arrest in the normal development of the frontonasal process. Disfigurement occurs when the frontonasal prominence remains in place. The forebrain retains its low overlying position and interferes with the normal converging movement of the optic placodes toward the midline. Hence, the eyes remain arrested in their "lateralised" embryonic settings [Fryburg et al., 1993].

FND is defined as a combination of two or more of the following clinical characteristics: true hypertelorbitism, broadening of nasal root; median facial cleft affecting the nose or both nose and upper lip and the palate, unilateral or bilateral clefting of the alae nasi, lack of formation of the nasal tip; anterior cranium bifidum occultum; and V-shaped hair prolongation onto the forehead generally over the area of cranium bifidum [Sedano et al., 1988].

There may be agenesis of the corpus callosum, midline skull defect, cleft lip and palate, ocular colobomata [Temple et al., 1990], and encephalocele [Verloes et al., 1992].

In CFND, the face is somewhat similar to that found in FND, but there is brachycephaly due to coronal synostosis [Sedano et al., 1988]. Frontal bossing, unilateral or bilateral hypertelorism, primary telecanthus, downslanting palpebral fissures, and exotropia are evident. Nasal root and bridge are broad and nasal tip mildly cleft. The maxillary dental arch is narrow and the midface is hypoplastic. Pterygium colli, hypoplasia of pectoral muscles, and umbilical hernia have also been reported [Webster and Deming, 1950; Reardon et al., 1990]. Skeletal anomalies have included asymmetric coronal synostosis, hypertelorism, hypoplastic nasal sinuses, hypoplastic nasal bone, thoracolumbar scoliosis, mild soft tissue syndactyly of digits, and longitudinally split nails of fingers and toes.

CLINICAL REPORT

B.P., a 13-year-old girl born to consanguineous parents, was referred because of frontal contour deformity and wide grooved nose. In her family history, there was no mention of other congenital anomalies. Pregnancy and labor were reportedly normal.

On physical examination, these anomalies were noted (Figs. 1–3): marked hypertelorbitism, left orbital dystopia, left convergent strabismus, hairy defect on the lateral half of right eyebrow with orbital ridge hypoplasia, broad nasal root and bifid nasal tip, asymmetric nostrils, depressed left dome, plagiocephalic appearance due to right coronal synostosis, macrostomia, high arched palate, and short lingual frenulum. In addition to the facial defects we also noted webbed neck with low posterior hairline, bilateral hypoplasia of the pectoralis major muscles like in Poland anomaly (Fig. 4), polythelia of the left breast, incomplete soft tis-

Received for publication April 11, 1995; revision received November 10, 1995.

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Fig. 1. Facial appearance of the patient. Note the bifid nose and left orbital dystopia, left convergent strabismus.

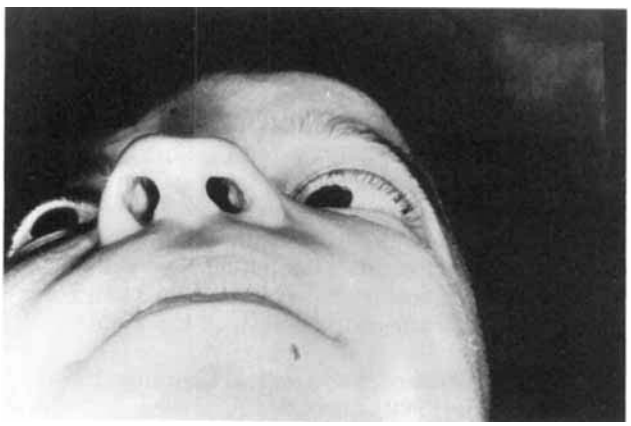

Fig. 2. Basal view. Note the frontal contour deformity.

Fig. 4. Anterior appearance of the patient. Bilateral pectoralis muscle hypoplasia and polythelia on left.

sue syndactyly between second and third fingers on right hand, mild clinodactyly of the third and fifth finger and shallow webs between all other fingers (Fig. 5), mild diastasis recti, and normal external genitalia. However, pelvic ultrasonographic evaluation showed bifid uterus.

Cranial CT scan was normal except for frontal deformity due to plagiocephaly. No facial clefts were noted that might explain facial appearance and hairy defect of eyebrow.

As a first-step correction we decided to approach the bifid nose which was the main complaint of the patient.

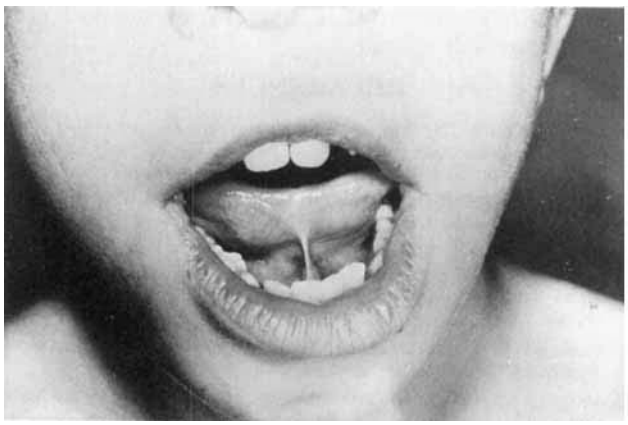

Fig. 3. Macrostomia and short lingual frenula.

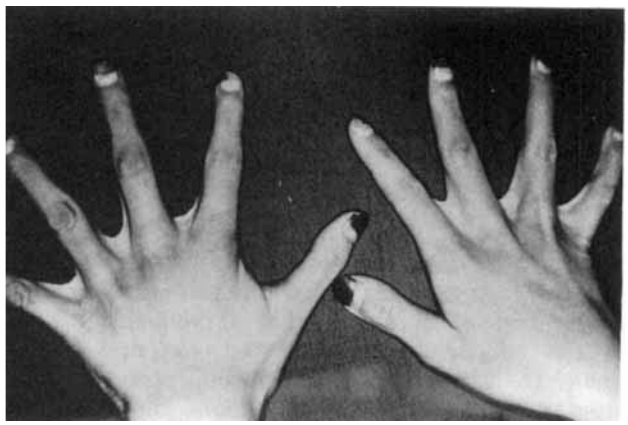

Fig. 5. Hands of the patient. Note the shallow web spaces

TABLE I. Comparison of the Present Case With Other Similar Cases

	Webster and Deming [1950]	Reardon et al. [1990]	Present case
Hypertelorism	+	+	+
Broad nasal root	+	+	+
Bifid nasal root	+	+	+
Ala nasi notching	+	+	—
Craniosynostosis	+	—	+
Webbed neck	+	—	+
Rounded shoulders	+	—	+
Pectoral muscle absent/hypoplastic	Bilaterally	Unilaterally	Bilaterally
Finger syndactyly	Bilaterally	Unilaterally	Unilaterally
Nail splitting	?	Unilaterally	—
Genital anomalies	?	?	+ (Bifid uterus)
Polythelia	?	?	+
Coarse and low set hair	?	?	+
Diastasis recti	?	?	+
High arched palate and short frenula	?	?	+

After transcartilaginous incision, the upper part of both lateral crura were dissected and elevated. Medial crura were sutured to each other as high as possible. Lateral crural cartilages were transferred to the opposite side of the rim, so that multiple cross-hatchings were done on the upper surfaces of these cartilages. Finally, acute angle of the tip was achieved and clefting of the nose disappeared.

DISCUSSION

Frontonasal malformation spectrum results from arrest in the normal development of the frontonasal process as a form of field defect. This alteration most likely occurs between days 21 and 70 of intrauterine life. CFND is probably due to premature and rapid neurocranial bone differentiation that leads to early fusion of cranial sutures [Sedano et al., 1988].

Darab et al. have experimentally produced various degrees of median facial clefting in mouse embryos by injecting methotrexate into female mice at about 9 days of pregnancy. Markedly dilated and congested blood vessels were found in the frontonasal process of affected embryos. This finding suggests that the development of frontonasal malformation spectrum may be due to damaged vessels in the frontonasal process and to distention of the developing brain rather than to alterations in neural crest cells [Darab et al., 1987]. Generalised or localized hypoxia resulting from ischemia secondary to vascular interruption is a potent nonspecific disruption factor [Grabowsky, 1970].

Bawinck and Weaver [1986] presented a hypothesis to explain the pathogenesis of the Poland, Klippel-Feil, Möbius and Sprengel anomalies, and isolated terminal transverse limb defect. These conditions are the result of an interruption of the early embryonic blood supply in the subclavian arteries, the vertebral arteries and/or their branches. The occlusions occur at specific sites in the vessels during or around the sixth week, i.e., during developing of the frontonasal process of embryonic development.

In 1950, Webster and Deming reported a case of bilateral pectoralis muscle hypoplasia and, in 1990, Reardon et al. reported Poland anomaly in association with CFND. Both CFND and the Poland anomaly are rare congenital defects.

The case reported by Webster and Deming [1950] concerned a girl with bilateral pectoralis muscle hypoplasia. She also had hypertelorism, broad nasal base with a bifid tip, and neck webbing. Her hands showed mild bilateral syndactyly. Coronal synostosis was confirmed roentgenographically in this case.

In addition, the case reported by Reardon et al. [1990] has marked hypertelorism, broad nasal root, bifid nasal tip, and right sided notching of the ala nasi. Additionally the pectoralis major muscle was absent on the right side, with ipsilateral 3–4 skin syndactyly of fingers.

The similarities of Webster and Deming [1950] and Reardon et al. [1990] cases to the present patient are apparent from the data summarised in Table I. It may be postulated that multiple artery supply disruption results in both Poland anomaly and CFND in the same patient. According to these findings and the literature review, we think that these cases might represent a new multiple congenital anomaly syndrome with craniofrontonasal dysplasia.

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